REMARKS

The Examiner rejected claims 1, 2, 4, 6-10, 12, and 14, while withdrawing claims 3, 5, 11, 13, and 15-32 from consideration. Claim 8 has been cancelled herein without prejudice. Thus, claims 1-7 and 9-32 remain pending.

As suggested by the Examiner, claims 1, 6, 8, 9, and 14 have been amended herein to recite that the polypeptide has higher affinity for morphine than for DAMGO. In addition, claims 9 and 14 have been amended to recite a recombinant cell as opposed to an isolated cell. Applicants note that these amendments to claims 1, 6, 8, 9, and 14, which do not narrow the scope of the claims, were made to clarify the claims as suggested by the Examiner. Claim 7 has been amended herein to change the transition term from "comprising" to "consisting essentially of." Applicants' specification fully supports these amendments. For example, page 2, lines 20-23 of Applicants' specification discloses that mu3 opiate receptors have higher affinity for morphine than for DAMGO. Likewise, the section starting on page 22, line 25 discloses making host cells containing isolated nucleic acid molecules. Thus, no new matter has been added.

In light of these amendments and the following remarks, Applicants respectfully request reconsideration and allowance of claims 1, 2, 4, 6, 7, 9, 10, 12, and 14.

Examiner Interviews

Applicants thank Examiner Landsman for the courtesy of the telephonic interview on April 5, 2005. The substance of this telephonic interview involved the issues and arguments presented herein. In particular, the Examiner suggested amending the claims to recite that the polypeptide has higher affinity for morphine than for DAMGO. The Examiner also asked Applicants to present arguments explaining the patentability of the claims and to point out that certain claims such as claims 6 and 7 encompass isolated nucleic acid molecules that can be used to detect nucleic acid encoding mu3 opiate receptors as opposed to nucleic acid encoding mu1 or mu2 receptors.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 1, 2, 4, 6-10, 12, and 14 under 35 U.S.C. § 112, first paragraph, as allegedly lacking an enabling disclosure. Applicants respectfully disagree. A person having ordinary skill in the art reading Applicants' specification would have been able to make and use the presently claimed invention without undue experimentation. From page 28, lines 7-15 of Applicants' specification, a person having ordinary skill in the art would have understood that the cloned human mu3 opiate receptor is a splice variant that includes replacing the last 12 amino acid residues of the human mu1 opioid receptor with 26 different amino acid residues. The nucleic acid sequence encoding these new 26 amino acid residues is set forth in SEQ ID NO:1. SEQ ID NO:4 contains the complete open reading frame of the cloned 2.0 kb insert. Thus, SEQ ID NO:4 contains human mu1/mu2 sequence followed by the sequence set forth in SEQ ID NO:1. A person having ordinary skill in the art also would have understood that other nucleic acids encoding a mu3 polypeptide can be obtained without undue experimentation. For example, common PCR cloning techniques similar to those disclosed in Example 1 can be used to obtain mu3 sequences from other species. Applicants note that the sequences for multiple mu1 and mu2 receptors were readily available, and Applicants' specification specifically teaches that mu3 opiate receptors are splice variants of mu1 and mu2 receptors. In fact, Applicants' specification discloses the location of the variant sequence which distinguishes mu1 and mu2 receptors from mu3 opiate receptors. Moreover, Applicants' specification discloses methods that can be used to determine whether or not a particular polypeptide has mu3 opiate receptor activity. For example, page 22, lines 17-23 discloses that:

> cells expressing a particular polypeptide can be analyzed to determine the polypeptide's binding affinity for morphine and DAMGO. If the binding affinity for morphine is higher than the binding affinity for DAMGO, then the expressed polypeptide has mu3 opiate receptor activity. Controls can be used to confirm the specificity of the various binding affinities. For example, cells lacking the polypeptide can be used to confirm that the measured binding affinity is specific for that particular polypeptide.

In light of the above, Applicants respectfully request withdrawal of this rejection of claims 1, 2, 4, 6-10, 12, and 14 under 35 U.S.C. § 112, first paragraph.

The Examiner also rejected claims 1, 2, 4, 6-10, 12, and 14 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a was as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicants respectfully disagree. A person having ordinary skill in the art reading Applicants' specification would have appreciated that Applicants invented the presently claimed isolated nucleic acid molecules that encode a polypeptide having mu3 opiate receptor activity. This is particularly true given that Applicants' specification discloses cloning mu3, a splice variant of mu1 that includes replacing the last 12 amino acid residues with 26 different amino acid residues. Applicants note that human mu1 is about 400 residues in length. Thus, a person having ordinary skill in the art would have appreciated from Applicants' specification that a common structural attribute of mu3 opiate receptors is the fact that a relatively short N-terminal end of mu3 receptors is different from mu1 receptors.

In addition, Applicants' specification contemplates and describes multiple nucleic acids molecules. For example, page 16, lines 17-21 disclose using common molecular cloning techniques such as site-directed mutagenesis to introduce deletions, insertions, or substitutions into nucleic acid sequences. The section extending from page 29, line 3 to page 31, line 15 discloses nucleic acids combining either human mu1 or human mu2 sequences with the 2.0 kb insert, while the section from page 31, line 16 to page 32, line 19 discloses a chimeric nucleic acid that combines rat mu2 with the human 2.0 kb insert. Moreover, Applicants' specification discloses methods that can be used to determine whether or not a particular polypeptide has mu3 opiate receptor activity. See, e.g., page 22, lines 17-23. Taken together, it is clear that a person having ordinary skill in the art reading Applicants' specification would have appreciated that Applicants invented the presently claimed subject matter. Thus, the present claims are adequately described.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 1, 2, 4, 6-10, 12, and 14 under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 1, 2, 4, 6-10, 12, and 14 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants respectfully disagree for the reasons of record. As suggested by the Examiner, however, claims 1, 6, 8, 9, and 14 have been amended herein to recite that the polypeptide has higher affinity for morphine than for DAMGO. Thus, this rejection is moot.

The Examiner also rejected claim 9 under 35 U.S.C. § 112, second paragraph, as being confusing in its recitation of an "isolated" cell, suggesting that the term "recombinant" cell would be clearer. As suggested by the Examiner, claims 9 and 14 have been amended herein to recite a recombinant cell. Thus, this rejection is moot.

Rejections under 35 U.S.C. § 102(a)

The Examiner rejected claims 6 and 7 under 35 U.S.C § 102(a) as being anticipated by the Birren *et al.* Accession Number AC027439.

Applicants respectfully disagree. The Birren *et al.* Accession Number AC027439 is a computer record that lists a working draft sequence of human chromosome 6. The note for this record stated the following on November 10, 2004:

> This is a "working draft" sequence. It currently consists of 18 contigs. The true order of the pieces is not known and their order in this sequence record is arbitrary. Gaps between the contigs are represented as runs of N, but the exact sizes of the gaps are unknown. This record will be updated with the finished sequence as soon as it is available and the accession number will be preserved.

Claims 6 and 7 recite isolated nucleic acid molecules. Page 7, lines 7-10 of Applicants' specification state that the "term 'isolated' as used herein with reference to nucleic acid refers to a naturally-occurring nucleic acid that is not immediately contiguous with both of the sequences with which it is immediately contiguous (one on the 5' end and one on the 3' end) in the naturally-occurring genome of the organism from which it is derived." None of the 18 contigs listed in the Birren *et al.* computer record is an isolated nucleic acid as presently claimed.

Applicants note that the sequence of SEQ ID NO:1 was found at nucleotides 33444 to 33524 of the working draft sequence.

Moreover, claim 6 recites that the isolated nucleic acid molecule does not hybridize to the sense or antisense strand of the sequence set forth in SEQ ID NO:12 or 13. SEQ ID NO:12 contains the nucleic acid sequence of human mu1, while SEQ ID NO:13 contains the nucleic acid sequence of human mu2. See, pages 33-35 of Applicants' specification. A Blast 2 Sequences alignment (http://www.ncbi.nlm.nih.gov/blast/bl2seq/bl2.html) reveals that most of both SEQ ID NOs:12 and 13 are within the sequence of the Birren *et al.* Accession Number. This is not unexpected since human mu1 and mu2 are found on human chromosome 6. Thus, the Birren *et al.* Accession Number does not anticipate claim 6.

Claim 7, as amended, recites a nucleic acid molecule consisting essentially of a nucleic acid sequence with a length and a percent identity to the sequence set forth in SEQ ID NO:1 over the length. The recited length is 15 to 81 nucleotides. At no point does the Birren *et al.* Accession Number disclose such a nucleic acid molecule. In fact, the nucleic acid disclosed in the Birren *et al.* Accession Number is 182048 nucleotides with many 100 nucleotide gaps. Applicants note that the sequence of SEQ ID NO:1 was found at nucleotides 33444 to 33524 of the working draft sequence. This region was apparently in a contig that was 8059 nucleotides in length. Thus, the Birren *et al.* Accession Number does not anticipate claim 7.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 6 and 7 under 35 U.S.C. § 102(a).

CONCLUSION

Applicants submit that claims 1, 2, 4, 6, 7, 9, 10, 12, and 14 are in condition for allowance, which action is requested. The Examiner is invited to call the undersigned attorney at the telephone number below if such will advance prosecution of this application. The Commissioner is authorized to charge any fees or credit any overpayments to Deposit Account No. 06-1050.

Respectfully submitted,

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